PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference 00398-155WO1	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/US2004/037201	International filing date *(day/month/year)* 05 November 2004 (05.11.2004)	Priority date *(day/month/year)* 05 November 2003 (05.11.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant NEW ENGLAND MEDICAL CENTER HOSPITALS, INC.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 08 May 2006 (08.05.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 740 14 35	Authorized officer Beate Giffo-Schmitt Telephone No. +41 22 338 87 20

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

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From the
INTERNATIONAL SEARCHING AUTHORITY

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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing (*day/month/year*)	29 JUN 2005
Applicant's or agent's file reference	FOR FURTHER ACTION See paragraph 2 below
00398-155WO1	

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US04/37201	05 November 2004 (05.11.2004)	05 November 2003 (05.11.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A01N 63/00; C12N 5/00, 5/06 and US Cl.: 424/93.1, 93.7, 93.71; 435/366, 372, 372.3

Applicant

NEW ENGLAND MEDICAL CENTER HOSPITALS, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☒ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/37201

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/37201

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 3-10,12-15,23	YES
	Claims 1,2,11,16-22,24	NO
Inventive step (IS)	Claims 7-9,23	YES
	Claims 1-6,10-22,24	NO
Industrial applicability (IA)	Claims 1-24	YES
	Claims NONE	NO

2. Citations and explanations:

Claims 1,2,11,16,22,24 lack novelty under PCT Article 33(2) as being anticipated by US 2003/0049696.

US 2003/0049696 discloses CD4+ CD25+ cells can be regulatory (Treg) or effector cells (see [0003]). US 2003/0049696 discloses Treg that are CD4+ CD25+ and positive or negative for a variety of other cell surface molecules (see [0022]). US 2003/0049696 discloses that said cells can be used to treat autoimmune disease [0025]) or transplant rejection (see [0025]) . Thus, whilst the reference does not disclose that said cells are ICOS positive, the Treg cells disclosed in US 2003/0049696 appear to encompass cells that express said markers (because the Treg are a subset of CD4+ CD25+ cells which are regulatory cells that suppress autoimmune disease and the ICOS positive cells recited in the claim are a subset of CD4+ CD25+ cells which are regulatory cells that suppress autoimmune disease. Thus, it is an inherent property of the Treg cells taught by US 2003/0049696 that said cells are ICOS positive.

Claims 17-21 lack novelty under PCT Article 33(2) as being anticipated by US 2002/0106730

US 2002/0106730 discloses the ICOS ligand human b7-H2 and the administration of said molecule to a patient to treat autoimmune disease (see [0016] and [0021]). US 2002/0106730 discloses that said molecule can be administered in the form of a cell expressing said molecule (see [0181])..

Claims 1-6,10-16,22,24 lack an inventive step under PCT Article 33(3) as being obvious over US 2003/0049696.

US 2003/0049696 discloses CD4+ CD25+ cells can be regulatory (Treg) or effector cells (see [0003]). US 2003/0049696 discloses Treg that are CD4+ CD25+ and positive or negative for a variety of other cell surface molecules (see [0022]). US 2003/0049696 discloses that said cells can be used to treat autoimmune disease [0025]) or transplant rejection (see [0025]) . Thus, whilst the reference does not disclose that said cells are ICOS positive, the Treg cells disclosed in US 2003/0049696 appear to encompass cells that express said markers (because the Treg are a subset of CD4+ CD25+ cells which are regulatory cells that suppress autoimmune disease and the ICOS positive cells recited in the claim are a subset of CD4+ CD25+ cells which are regulatory cells that suppress autoimmune disease. GVHD is an art known form of transplantation rejection. It would have been obvious to use any art known therapeutic agent(s) in combination with the administered Treg to treat autoimmune disease or transplant rejection (such as ECP, CsA, antibody therapy, etc).

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/37201

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 7-9 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because of the claims 7-9 are not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because of the following reasons. US 2003/0049696 discloses in section [0055] that in order to treat cancers it s necessary to block Treg (suppressor cells encompassed by the claimed cells) that suppress antitumor responses. Thus, Treg could not be used to treat cancer because they block antitumor immune responses.